

Image

PTO/SB/21 (88-03)
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TRANSMITTAL FORM <i>(to be used for all correspondence after initial filing)</i>	Application Number	09/715,983
	Filing Date	November 20, 2000
	First Named Inventor	Brett P. Monia
	Art Unit	1635
	Examiner Name	Jane J. Zara
Total Number of Pages in This Submission	Attorney Docket Number	ISIS0057-100/ISPH-0519

ENCLOSURES (check all that apply)		
<input checked="" type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment / Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/ Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input checked="" type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s)	<input type="checkbox"/> After Allowance Communication to Group <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) <i>(please identify below):</i> 1. Exhibit A: Final Rejection Mailed 5/7/03 2. Exhibit B: Amendment and request for Reconsideration filed 7/7/03 3. Exhibit C: Advisory Action mailed 7/30/03 4. Exhibit D: Amendment mailed 8/7/03 5. Exhibit E: Return Card stamped by PTO 6. Exhibit F: Amendment Originally filed on 8/7/03, a Notice of Appeal, and an Extension of time Filed 11/7/03

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT	
Firm or Individual name	Paul K. Legaard/ 38,534
Signature	
Date	November 7, 2003

CERTIFICATE OF MAILING			
I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.			
Typed or printed name	Paul K. Legaard/38,534		
Signature		Date	November 7, 2003

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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**FEE TRANSMITTAL
for FY 2004**

Effective 10/01/2003. Patent fees are subject to annual revision.

☒ Applicant claims small entity status. See 37 CFR 1.27**TOTAL AMOUNT OF PAYMENT** (\$) 130.00**Complete if Known**

Application Number	09/715,983
Filing Date	November 20, 2000
First Named Inventor	Brett P. Monia
Examiner Name	Jane J. Zara
Art Unit	1635
Attorney Docket No.	ISIS0057-100/ISPH-0519

METHOD OF PAYMENT (check all that apply)☐ Check ☐ Credit card ☐ Money ☐ Other ☐ None
Order☒ Deposit Account:Deposit
Account
Number

50-1275

Deposit
Account
Name

The Director is authorized to: (check all that apply)

☒ Charge fee(s) indicated below ☒ Credit any overpayments
☒ Charge any additional fee(s) during the pendency of this application
☐ Charge fee(s) indicated below, except for the filing fee
to the above-identified deposit account.**FEE CALCULATION****1. BASIC FILING FEE****Large Entity** **Small Entity**

Fee Code	Fee (\$)	Fee Code	Fee (\$)	Fee Description	Fee Paid
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1)

(\$ 0)

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

	Extra Claims	Fee from below	Fee Paid
Total Claims	- ** =	X	=
Independent Claims	- ** =	X	=
Multiple Dependent		X	=

Large Entity **Small Entity**

Fee Code	Fee (\$)	Fee Code	Fee (\$)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2)

(\$ 0)

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)**3. ADDITIONAL FEES****Large Entity** **Small Entity**

Fee Code	Fee (\$)	Fee Code	Fee (\$)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet.	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	
1402	330	2402	165	Filing a brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,330	2453	665	Petition to revive - unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	130
1807	50	1807	50	Processing fee under 37 CFR 1.17 (q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR § 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR § 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify)

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3)

(\$ 130.00)

SUBMITTED BY**Complete (if applicable)**

Name (Print/Type)	Paul K. Legaard	Registration No. (Attorney/Agent)	38,534	Telephone	215-665-6914
Signature				Date	November 7, 2003

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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DOCKET NO.: ISIS0057-100 (ISPH-0519)

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors: **Monia, Cowsert, Murray, Butler, and Dean**

Serial No.: **09/715,983**

Group Art Unit: **1635**

Filed: **November 20, 2000**

Examiner: **J. Zara**

Title: **Antisense Modulation Of PI3K P85 Expression**

I certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

On 07 November 2003


Paul K. Legaard Reg. No. 38,534

Mail Stop Petition
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Dear Sir:

PETITION TO THE COMMISSIONER UNDER 37 CFR §1.182

Applicants respectfully request a refund of fees paid on November 7, 2003 in connection with the above-identified application. The present Petition is accompanied by the authorization to charge the Deposit Account the appropriate fee of \$130.00.

Statement of Facts Involved

1. The U.S. Patent and Trademark Office (PTO) mailed a Final Rejection on May 7, 2003 in which claims 24-31 and 40-47 were rejected for lack of enablement (see Exhibit A, enclosed herewith).

2. Applicants' representative filed via Express Mail an "Amendment and Request for Reconsideration" on July 7, 2003 (see Exhibit B, enclosed herewith).

11/12/2003 SLUANG1 00000059 501275 09715983
01 FC:1460 130.00 DA

3. The PTO mailed an Advisory Action on July 30, 2003 which indicated that: 1) Applicants' reply dated July 7, 2003 overcame the enablement rejections of claims 24, 26-28, 30, and 31 (i.e., the only rejection of those claims); and 2) amended claims 24, 26-28, 30, and 31 would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s) (see Exhibit C, enclosed herewith).

4. Applicants' representative filed via Express Mail, along with a return card, an "Amendment" on August 7, 2003 in which the non-allowed claims were canceled -- only the allowable claims (i.e., claims 24, 26-28, 30, and 31) remained pending (see Exhibit D, enclosed herewith).

5. Applicants' representative received a copy of the return card on August 19, 2003 which showed that the PTO received Applicants' Amendment mailed August 7, 2003 as indicated by the PTO date stamp (see Exhibit E, enclosed herewith).

6. On November 6, 2003, Applicants' undersigned representative spoke with Examiner John LeGuyader regarding Facts 1-5 listed above. Examiner LeGuyader indicated that the PTO had no record of receiving the Amendment filed August 7, 2003. Examiner LeGuyader referred Applicants' undersigned representative to Examiner Andrew Wang.

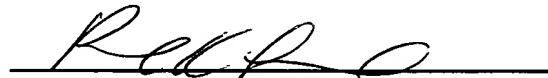
7. On November 6, 2003, Applicants' undersigned representative spoke with Examiner Andrew Wang regarding Facts 1-6 listed above. Examiner Wang indicated that the above-identified application was in the process of being scanned. Examiner Wang further suggested that, in view of Facts 1-5 above, Applicants' undersigned representative timely file a copy of the Amendment originally filed on August 7, 2003, a Notice of Appeal, and an Extension of Time in order to prevent abandonment of the Application.

8. Applicants' undersigned representative filed via Express Mail on November 7, 2003 a copy of the Amendment originally filed on August 7, 2003, a Notice of Appeal, and an Extension of Time (see Exhibit F, enclosed herewith).

Action Requested

The facts above indicate that Applicants timely filed (i.e., within three months of the date of the Final Rejection -- on August 7, 2003) an Amendment which, if entered, would result in only allowable claims remaining pending. The facts above also indicate that the PTO, in fact, received the Amendment filed August 7, 2003. Thus, all fees that were paid on November 7, 2003 (i.e., the Notice of Appeal fee of \$165.00 and the Extension of Time fee of \$475.00, totaling \$640.00) were so paid on account of PTO error/delay. Accordingly, Applicants respectfully request that they receive a refund of \$640.00. Further, Applicants respectfully request that their patent term adjustment not be negated by the PTO error/delay in issuing a Notice of Allowance.

Respectfully submitted,



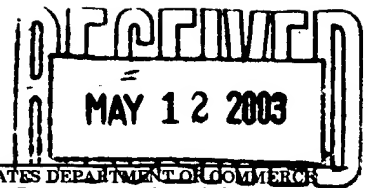
Paul K. Legaard
Registration No. 38,534

Date: 7 November 2003

COZEN O'CONNOR
1900 Market Street
Philadelphia, PA 19103-3508
Telephone: (215) 665-6914
Facsimile: (215) 701-2141



UNITED STATES PATENT AND TRADEMARK OFFICE



6304

Exhibit A

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,983	11/20/2000	Brett P. Monia	ISPH-0519	6803

7590

05/07/2003

Kathleen A. Tyrrell
Licata & Tyrrell P.C.
66 E. Main Street
Marlton, NJ 08053

EXAMINER

ZARA, JANE J

ART UNIT	PAPER NUMBER
----------	--------------

1635

DATE MAILED: 05/07/2003

8/7/03

(MAX400A) 11/7/03

(NOT IN system yet)

Please find below and/or attached an Office communication concerning this application or proceeding.

RECEIVED
COZEN IP DEPT.

MAY 14 2003

DUE DATE 8/7/2003
MAX DATE 11/7/2003
DOCKETED BY JNL

FINAL REJECTION

Office Action Summary

Application No.
09/715,983

Applicant(s)
Monia et al

Examiner
Jane Zara

Art Unit
1635



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Feb 20, 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24-31 and 40-47 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24-31 and 40-47 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ | 6) <input type="checkbox"/> Other: |

App

Art Unit: 1635

DETAILED ACTION

This Office action is in response to the communication filed February 20, 2003, Paper No.

10.

Claims 24-31, 40-47 are pending in the instant application.

Any rejections not repeated in this Office action are hereby withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Maintained Rejections

Claims 24-31 and 40-47 are rejected under 35 U.S.C. 112, first paragraph, for lacking enablement over the scope claimed for the reasons of record set forth in the Office action mailed November 19, 2002, Paper No. 9.

Applicant's arguments filed February 20, 2003 have been fully considered but they are not persuasive. Applicants argue that the full scope of the claims is enabled, which scope comprises decreasing blood glucose and insulin levels in any organism comprising the administration of antisense oligonucleotides between 8-30 nucleobases in length, which antisense specifically target and inhibit the expression of human PI3K p85 of SEQ ID NO: 1. Contrary to Applicants assertions, however, the instant disclosure teaches the ability to decrease blood glucose and insulin levels using mouse models, which models are reasonable for analogous treatment

Art Unit: 1635

applications in humans. The ability to achieve these treatment effects in mice, as well as knowing the homology between mouse and human PI3K p85, however, is not necessarily predictive of the ability to achieve these treatment effects in any and/or all organisms comprising the administration of antisense oligonucleotides that specifically target and inhibit the expression of human PI3K p85 of SEQ ID NO: 1.

Applicants additionally argue that the full scope of the claims are enabled, including the ability to prevent or delay onset of increased blood glucose or insulin levels in any organism comprising the administration of antisense oligonucleotides between 8 and 30 nucleobases that specifically target and inhibit the expression of PI3K p85 of SEQ ID NO: 1, because well designed pharmacological studies in vivo in animals are predictive of the production of the same effects in humans, including rodent models for blood glucose and insulin responses in humans.

The correlation or appropriateness of the animal models provided in the instant application for predicting efficacy in humans for purposes of enablement is not the issue or issues addressed in the instant scope of enablement rejection. Contrary to Applicants' assertions, no evidence has been provided in the instant disclosure or in the known scientific literature, for the ability to delay the onset or prevent increased blood glucose or insulin levels in an organism comprising the administration of antisense that target and specifically inhibit the expression of PI3K p85. The instant disclosure provides evidence for the ability to decrease blood glucose levels or insulin levels in mice comprising administration of antisense between 8-30 nucleobases that specifically target and inhibit the expression of human PI3K p85. The ability to decrease blood glucose levels

Art Unit: 1635

or insulin levels in an organism (i.e mouse or humans) comprising the administration of these antisense, however, is not predictive of the ability to delay the onset or prevent increasing blood glucose or insulin levels. The treatment effects demonstrated are not extrapolatable to prevention. It would require undue experimentation beyond that which has been provided in the instant disclosure, or which exists in the art, to prevent or delay the onset of increasing blood glucose or insulin levels in any organism comprising the administration of antisense. Therefore, the claimed invention is not enabled for this broad scope.

Conclusion

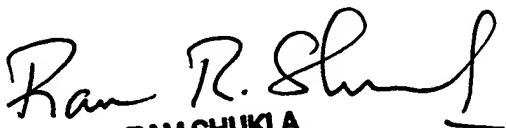
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Art Unit: 1635

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is (703) 306-5820. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.


RAM SHUKLA
PRIMARY EXAMINER

JZ

May 4, 2003

Exhibit B



EV 146602115 US



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Label 11-F October 2001

Post Office To Address

ORIGIN (POSTAL USE ONLY)			
PO ZIP Code 19104	Day of Delivery <input type="checkbox"/> Next <input checked="" type="checkbox"/> Second	Flat Rate Envelope <input type="checkbox"/>	
Date In 7-7-3	<input checked="" type="checkbox"/> 12 Noon <input type="checkbox"/> 3 PM	Postage \$ 13.65	
Mo. Day Year 7-7-3	<input checked="" type="checkbox"/> Military	Return Receipt Fee	
Time In 7:59	<input type="checkbox"/> 2nd Day <input type="checkbox"/> 3rd Day	COD Fee	
Weight 4 lbs. 4 ozs.	Int'l Alpha Country Code	Insurance Fee	
No Delivery <input type="checkbox"/> Weekend <input type="checkbox"/> Holiday	Acceptance Clerk Initials [Signature]	Total Postage & Fees \$ 13.65	

DELIVERY (POSTAL USE ONLY)		
Delivery Attempt	Time	Employee Signature
Mo. Day	<input type="checkbox"/> AM <input type="checkbox"/> PM	
Delivery Attempt	Time	Employee Signature
Mo. Day	<input type="checkbox"/> AM <input type="checkbox"/> PM	
Delivery Date	Time	Employee Signature
Mo. Day	<input type="checkbox"/> AM <input type="checkbox"/> PM	
<input type="checkbox"/> WAVES OF SIGNATURE (Domestic Only) Additional merchandise insurance is void if waiver of signature is requested. I wish delivery to be made without obtaining signature of addressee or addressee's agent (if delivery employee judges that article can be left in secure location) and I authorize that delivery employee's signature constitutes valid proof of delivery.		
NO DELIVERY <input type="checkbox"/> Weekend <input type="checkbox"/> Holiday		
Customer Signature		

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Federal Agency Acct. No. or Postal Service Acct. No.

FROM: (PLEASE PRINT) PHONE ()

COZEN O'CONNOR
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ONguyen/Hope Graves
ISIS0057-100 (136661.000)

TO: (PLEASE PRINT) PHONE ()

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U.S. Patent and Trademark Office
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

**RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP NO. 1635**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: **Monia et al.**

Confirmation No. **6803**

Serial No.: **09/715,983**

Group Art Unit: **1635**

Filed: **November 20, 2000**

Examiner: **Zara, Jane J.**

Title: **Antisense Modulation of PI3K P85 Expression**

EXPRESS MAIL INFORMATION

**EXPRESS MAIL LABEL NO: EV146 602 115US
DATE OF DEPOSIT: July 7, 2003**

MAIL STOP AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

AMENDMENT AND REQUEST FOR RECONSIDERATION

In response to the Final Rejection mailed May 7, 2003, Applicants respectfully request that the following amendments be entered and that the rejection of claims in the application be reconsidered and withdrawn.

IN THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Please cancel claims 25, 29, 41 and 45 without prejudice.

Please amend claims 24, 27, 28, 31, 40, 43, 44 and 47 as follows.

24. (Currently Amended) A method of decreasing blood glucose levels in ~~an animal~~ a human comprising administering to said ~~animal~~ human an antisense compound 8 to 30 nucleobases in length targeted to a nucleic acid molecule of SEQ ID NO: 1 encoding human PI3K p85, wherein said compound specifically hybridizes with and inhibits the expression of human PI3K p85.

25. (Canceled)

26. The method of claim 24 wherein the blood glucose levels are plasma glucose levels or serum glucose levels.

27. (Currently Amended) The method of claim 24 wherein the ~~animal~~ human is a diabetic ~~animal~~ human.

28. (Currently Amended) A method of decreasing insulin levels in ~~an animal~~ a human comprising administering to said ~~animal~~ human an antisense compound 8 to 30 nucleobases in length targeted to a nucleic acid molecule of SEQ ID NO: 1 encoding human PI3K p85, wherein said compound specifically hybridizes with and inhibits the expression of human PI3K p85.

29. (Canceled)

30. The method of claim 28 wherein the insulin levels are plasma insulin levels or serum insulin levels.

31. (Currently Amended) The method of claim 28 wherein the ~~animal~~ human is a diabetic ~~animal~~ human.

40. (Currently Amended) A method of preventing or delaying the onset of an increase in blood glucose levels in ~~an animal~~ a human comprising administering to said ~~animal~~ human an antisense

compound 8 to 30 nucleobases in length targeted to a nucleic acid molecule of SEQ ID NO: 1 encoding human PI3K p85, wherein said compound specifically hybridizes with and inhibits the expression of human PI3K p85.

41. (Canceled)

42. (Currently Amended) The method of claim 40 wherein the blood glucose levels are plasma glucose levels or serum glucose levels.

43. The method of claim 40 wherein the ~~animal~~ human is a diabetic ~~animal~~ human.

44. (Currently Amended) A method of preventing or delaying the onset of an increase in insulin levels in ~~an animal~~ a human comprising administering to said ~~animal~~ human an antisense compound 8 to 30 nucleobases in length targeted to a nucleic acid molecule of SEQ ID NO: 1 encoding human PI3K p85, wherein said compound specifically hybridizes with and inhibits the expression of human PI3K p85.

45. (Canceled)

46. The method of claim 44 wherein the insulin levels are plasma insulin levels or serum insulin levels.

47. (Currently Amended) The method of claim 44 wherein the ~~animal~~ human is a diabetic ~~animal~~ human.

REMARKS

Claims 24-31 and 40-47 are pending, and are rejected. Claims 24, 27, 28, 31, 40, 43, 44 and 47 have been amended to recite "human" instead of "animal" to further clarify the claims. Claims 25, 29, 41 and 45 recite "wherein the animal is a human" and have been canceled. No new matter has been added.

Upon entry of this amendment, claims 24, 26-28, 30, 31, 40, 42-44, 46 and 47 will be pending.

I. The Claimed Invention Is Sufficiently Enabled**A. Decreasing glucose/insulin levels**

Claims 24-31 and 40-47 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to provide an enabling disclosure. Claims 25, 29, 41 and 45 have been canceled. Applicants traverse the rejections and request reconsideration of the same.

The Office Action asserts that although the claims drawn to decreasing blood glucose and/or insulin levels in humans are allowable, undue experimentation is required to decrease blood glucose and/or insulin levels in other animals. Although Applicants disagree, solely to advance prosecution of the present application, claims 24, 27, 28, 31, 40, 43, 44 and 47 have been amended to recite “human” instead of “animal”. Accordingly, claims 24, 27, 28, 31, 40, 43, 44 and 47 are fully enabled. Furthermore, claims 26, 30, 42 and 46 depend from claims 24, 28, 40 and 44, respectively, and are also similarly enabled because these claims also recite “human”.

The Examiner additionally rejected claims 40, 42-44, 46 and 47, which recite a method of “preventing or delaying” the onset of an increase in blood glucose or insulin, stating that the ability to decrease blood glucose levels or insulin levels in an organism comprising the administration of these antisense is not predictive of the ability to delay the onset or prevent increasing blood glucose or insulin level, and the “treatment effects demonstrated are not extrapolatable to prevention.” (See pages 3 and 4 of the Office Action). Applicants respectfully disagree and assert that claims 40, 42-44, 46 and 47 are fully enabled by the specification.

The enablement requirement of §112 is satisfied so long as a disclosure contains sufficient information that persons of ordinary skill in the art having the disclosure before them would be able to make and use the invention. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) (the legal standard for enablement under §112 is whether one skilled in the art would be able to practice the invention without undue experimentation). In this respect, the following statement from *In re Marzocchi*, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971), is noteworthy:

The only relevant concern of the Patent Office under these circumstances should be over the truth of any such assertion. The first paragraph of §112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.

As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the

invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must** be taken as in compliance with the enabling requirements of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied upon for enabling support. (emphasis added).

Throughout the specification, Applicants have clearly taught that an onset of an increase in glucose and/or insulin levels may be prevented or delayed, and how such prevention or delay may be achieved. For example, Applicants have shown that the inhibition of nucleic acid molecules expressing PI3K p85 reduces glucose and insulin levels in vivo. (See Examples 21 and 22 of the specification). Since it has been shown that the decrease in expression of PI3K p85 correlates with the decrease in glucose and insulin levels, one of ordinary skill would expect that a increase in the level of expressed PI3K p85 would correlate with a increase in the level of glucose and insulin. Thus, a reasonable “extrapolation” can be made that if an antisense compound of claims 40, 42-44, 46 and 47 is administered to inhibit the expression of PI3K p85, the level of PI3K p85 would not be able to increase, and accordingly, an increase in the level of glucose and insulin would be **prevented or delayed**. Therefore, one of ordinary skill would understand that the present invention teaches that an onset of an increase in glucose and/or insulin may be prevented or delayed. Indeed, Applicants have shown that blood glucose and/or insulin levels can be decreased upon administration of a compound of the invention. Accordingly, there is no reason to believe that continued administration of the compounds would not prevent or delay an increase of blood glucose and/or insulin levels.

Throughout the specification, Applicants have also enabled one of ordinary skill to prevent or delay the increase in glucose and/or insulin. For example, Applicants taught that the present invention provides for “methods of treating an animal, particularly a human, suspected of having or being prone to a disease or condition associated with expression of PI3K p85 by administering a therapeutically or **prophylactically** [i.e., preventing or delaying] effective amount of one or more of the antisense compounds...of the invention [i.e. the antisense compounds recited in claims 40, 42-44, 46 and 47]. (See page 5 of the specification). Moreover, Applicants taught that the claimed compounds may be administered in a number of ways, e.g., topical, inhalation, intratracheal, intranasal, epidermal, etc. (see page 23 of the specification); and

the dosage can be determined by one of ordinary skill in the art, e.g., 0.01 ug to 100 g per kg of body weight (see page 47 of the specification).

Additionally, the Applicants even clearly provided examples of how to practice the claimed methods of preventing an onset of an increase of glucose and/or insulin. For example, on page 47 of the specification, Applicants taught that:

“Following successful treatment, it may be desirable to have the patient undergo maintenance therapy to prevent the recurrence of the disease state, wherein the oligonucleotide is administered in maintenance doses, ranging from 0.01 ug to 100 g per kg of body weight, once or more daily...”

Applicants submit that there is no reason to doubt the objective truth of the statements contained in the application. Therefore, the Examiner **must** take Applicants’ teaching of methods of preventing or delaying the onset of increase in glucose and/or insulin level as being in compliance with the enabling requirements of the first paragraph of §112. *In re Marzocchi*, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971).

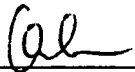
Thus, claims 40, 42-44, 46 and 47 are fully enabled. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

II. Conclusion

Pending claims 24, 26-28, 30, 31, 40, 42-44, 46 and 47 are in condition for allowance and an early notice of the same is earnestly solicited. If, for any reason, the present application fails to proceed to allowance, the Examiner is encouraged to contact Applicants' undersigned representative at (215) 665-2158.

Respectfully submitted,

Dated: July 7, 2003



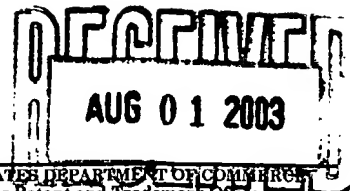
Quan L. Nguyen
Reg. No. 46,957

COZEN O'CONNOR, P.C.
1900 Market Street, 5th Floor
Philadelphia, PA 19103-3508
Telephone: (215) 665-2158
Facsimile: (215) 701-2057

Doc No. 1874474 v.1



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Exhibit C

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/715,983	11/20/2000	Brett P. Monia	ISPH-0519	6803

7590
Kathleen A. Tyrrell
Licata & Tyrrell P.C.
66 E. Main Street
Marlton, NJ 08053

07/30/2003

8/4/03
COPY SENT TO CLIENT

EXAMINER

ZARA, JANE J

ART UNIT PAPER NUMBER

1635

DATE MAILED: 07/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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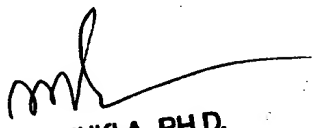
DUE DATE 7/7/2003
MAX DATE 7/7/2003
DOCKETED BY JNL

Application/Control Number: 09/715,983

Art Unit: 1635

Attachment

Claims 40, 42-44, 46 and 47 are rejected for lacking enablement over the scope claimed for the reasons of record set forth previously in the Office actions mailed November 19, 2002 and May 7, 2003, Paper Nos. 9 and 11 respectively. Applicants argue that it would not be unpredictable to prevent or delay the onset of increasing insulin or blood glucose levels in a human comprising administration of antisense targeting PI3K p85 because the instant disclosure teaches a decrease in blood glucose or insulin levels in appropriate mouse models, and the extrapolation from decreasing blood glucose or insulin levels in a mouse model for up to two weeks following weekly administration of antisense, to prevention of any and/or all increases in blood glucose or insulin levels for an undefined period following administration of antisense is reasonable. Contrary to Applicants' arguments, the observed decrease in blood glucose or insulin levels following administration of antisense is not predictive of the ability to prevent or delay increasing blood glucose or insulin levels in an organism for an undefined period of time comprising administration of anti- PI3K p85 antisense. Therefore the enablement rejection is maintained.



RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER

Advisory Action

Application No.
09/715,983

Applicant(s)
Monia et al

Examiner
Jane Zara

Art Unit
1635



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED Jul 7, 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see NOTE below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☒ Applicant's reply has overcome the following rejection(s):
Scope of enablement rejections of claims 24, 26-28, 30, 31
4. ☒ Newly proposed or amended claim(s) 24, 26-28, 30, and 31 would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
Please see attached. The enablement rejection is maintained for claims 40, 42-44, 46 and 47.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
- The status of the claim(s) is (or will be) as follows:
- Claim(s) allowed: 24, 26-28, 30, and 31
- Claim(s) objected to: None
- Claim(s) rejected: 40, 42-44, 46, and 47
- Claim(s) withdrawn from consideration: _____
8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
10. ☐ Other: _____

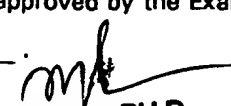

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER

Exhibit D

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ISIS0057-10-0 (ISPH-0519)/136661.000

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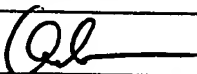
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TRANSMITTAL FORM (to be used for all correspondence after initial filing)		Application Number	09/715,983
		Filing Date	November 20, 2000
		First Named Inventor	Brett P. Monia et al.
		Art Unit	1635
		Examiner Name	Jane J. Zara
Total Number of Papers in This Submission	One	Attorney Docket Number	ISIS0057-100 (ISPH-0519)

ENCLOSURES (check all that apply)		
<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input checked="" type="checkbox"/> Amendment / Response <input checked="" type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Assignment Papers (for an Application) <input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s)	<input type="checkbox"/> After Allowance Communication to Group <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input type="checkbox"/> Other Enclosure(s) (please identify below):
Remarks Express Mail Label No. EV146 607 656US Date of Deposit: August 7, 2003		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT	
Firm or Individual name	Quan Le Nguyen, Reg. No. 46,957 Cozen O'Connor, P.C.
Signature	
Date	August 7, 2003

CERTIFICATE OF MAILING			
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as Express Mail Service in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.			
Typed or printed name	Quan L. Nguyen, Reg. No. 46,957		
Signature		Date	August 7, 2003

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commission r for Patents, P.O. B x 1450, Alexandria, VA 22313-1450.

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DOCKET NO: ISIS0057-100 (ISPH-0519)

PATENT

**RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP NO. 1635**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: **Monia et al.**

Confirmation No. **6803**

Serial No.: **09/715,983**

Group Art Unit: **1635**

Filed: **November 20, 2000**

Examiner: **Zara, Jane J.**

Title: **Antisense Modulation of PI3K P85 Expression**

EXPRESS MAIL INFORMATION

**EXPRESS MAIL LABEL NO: EV 146 607 656 US
DATE OF DEPOSIT: August 7, 2003**

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P.O. Box 1450
Alexandria, VA 22313-1450**

Dear Sir:

AMENDMENT

In response to the Advisory Action mailed July 30, 2003, and Final Rejection mailed May 7, 2003, Applicants respectfully request that the following amendments be entered.

IN THE CLAIMS:

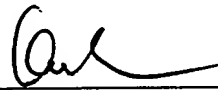
Please cancel claims 40, 42-44, 46 and 47 without prejudice.

REMARKS

Claims 24, 26-28, 30, 31, 40, 42-44, 46 and 47 are be pending. Claims 40, 42-44, 46 and 47 have been canceled. Upon entry of the amendment, claims 24, 26-28, 30 and 31 will remain pending.

In the Advisory Action mailed July 30, 2003, the Examiner indicated that claims 24, 26-28, 30 and 31 are allowable if submitted in a separate, timely filed amendment canceling non-allowable claims. Although Applicants maintain that claims 40, 42-44, 46 and 47 are also allowable, to expedite the prosecution of the application, Applicants have canceled non-allowable claims 40, 42-44, 46 and 47. Applicants respectfully request that the Examiner issue claims 24, 26-28, 30 and 31.

Respectfully submitted,



Quan L. Nguyen
Reg. No. 46,957

Dated: August 7, 2003

COZEN O'CONNOR, P.C.
1900 Market Street, 5th Floor
Philadelphia, PA 19103-3508
Telephone: (215) 665-2158
Facsimile: (215) 701-2057

IN THE CLAIMS:

Please cancel claims 40, 42-44, 46 and 47 without prejudice.


REMARKS

Claims 24, 26-28, 30, 31, 40, 42-44, 46 and 47 are be pending. Claims 40, 42-44, 46 and 47 have been canceled. Upon entry of the amendment, claims 24, 26-28, 30 and 31 will remain pending.

In the Advisory Action mailed July 30, 2003, the Examiner indicated that claims 24, 26-28, 30 and 31 are allowable if submitted in a separate, timely filed amendment canceling non-allowable claims. Although Applicants maintain that claims 40, 42-44, 46 and 47 are also allowable, to expedite the prosecution of the application, Applicants have canceled non-allowable claims 40, 42-44, 46 and 47. Applicants respectfully request that the Examiner issue claims 24, 26-28, 30 and 31.

Respectfully submitted,

Dated: August 7, 2003



Quan L. Nguyen
Reg. No. 46,957

COZEN O'CONNOR, P.C.
1900 Market Street, 5th Floor
Philadelphia, PA 19103-3508
Telephone: (215) 665-2158
Facsimile: (215) 701-2057

Exhibit E

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AND TRADEMARK OFFICE**

Paper: Transmittal Form for Amendment After Final (w/Express Mail Service); Amendment After Final in response to Final Rejection dated May 7, 2003; Return Postcard all via Express Mail No. EV146 607 656US

Applicant(s): Brett P. Monia et al.

Title: ANTISENSE MODULATION OF PI3K P85 EXPRESSION

Serial No.: 09/715,983

Filed: November 20, 2000

EV146607656US

Docket No.: ISIS0057-100 (ISPH-0519)

Date Sent: August 7, 2003

QLNguyen/Hope Graves

**RECEIVED IN THE UNITED STATES PATENT
AND TRADEMARK OFFICE**

Paper: Transmittal Form for Amendment After Final (w/Express Mail Service); Amendment After Final in response to Final Rejection dated May 7, 2003; Return Postcard all via Express Mail No. EV146 607 656US

Applicant(s): Brett P. Monia et al.

Title: ANTISENSE MODULATION OF PI3K P85 EXPRESSION

Serial No.: 09/715,983

Filed: November 20, 2000

Docket No.: ISIS0057-100 (ISPH-0519)

Date Sent: August 7, 2003

AUG 19 2003
QLNguyen/Hope Graves

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Exhibit F

PTO/SB/21 (08-03)

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TRANSMITTAL
FORM

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Application Number	09/715,983		
	Filing Date	November 20, 2000	
	First Named Inventor	Brett P. Monia	
	Art Unit	1635	
	Examiner Name	Jane J. Zara	
Total Number of Pages in This Submission		Attorney Docket Number	ISIS0057-100/ISPH-0519

ENCLOSURES (check all that apply)

<input checked="" type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment / Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input checked="" type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s)	<input type="checkbox"/> After Allowance Communication to Group <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input checked="" type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): 1. Copy of return Post Card Stamped by the USPTO for Amendment filed 8/7/03. 2. Copy of Express Mail Label for Amendment filed 8/7/03. 3. Copy of Transmittal for Amendment filed on 8/7/03. 4. Copy of Amendment filed 8/7/03 in response to Advisory Action dated 7/30/03.
Remarks Express Mail No.: EL 964553545 US Date of Deposit: November 7, 2003		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Paul K. Legaard/ 38,534
Signature	
Date	November 7, 2003

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.			
Typed or printed name	Paul K. Legaard/38,534		
Signature		Date	November 7, 2003

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time

FEE TRANSMITTAL for FY 2004

Effective 10/01/2003. Patent fees are subject to annual revision.

☒ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$) 640.00

Complete If Known

Application Number 09/715,983
Filing Date November 20, 2000
First Named Inventor Brett P. Monia
Examiner Name Jane J. Zara
Art Unit 1635
Attorney Docket No. ISIS0057-100/ISPH-0519

METHOD OF PAYMENT (check all that apply)

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☒ Deposit Account:

Deposit Account Number 50-1275

Deposit Account Name

The Director is authorized to: (check all that apply)

☒ Charge fee(s) indicated below ☒ Credit any overpayments
☒ Charge any additional fee(s) during the pendency of this application
☐ Charge fee(s) indicated below, except for the filing fee to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity		Small Entity		Fee Description	Fee Paid
Fee Code	Fee (\$)	Fee Code	Fee (\$)		
1001	770	2001	385	Utility filing fee	
1002	340	2002	170	Design filing fee	
1003	530	2003	265	Plant filing fee	
1004	770	2004	385	Reissue filing fee	
1005	160	2005	80	Provisional filing fee	

SUBTOTAL (1)

(\$ 0)

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

Total Claims	Extra Claims	Fee from below	Fee Paid
Independent Claims			
Multiple Dependent			

Large Entity		Small Entity		Fee Description
Fee Code	Fee (\$)	Fee Code	Fee (\$)	
1202	18	2202	9	Claims in excess of 20
1201	86	2201	43	Independent claims in excess of 3
1203	290	2203	145	Multiple dependent claim, if not paid
1204	86	2204	43	** Reissue independent claims over original patent
1205	18	2205	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2)

(\$ 0)

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity		Small Entity		Fee Description	Fee Paid
Fee Code	Fee (\$)	Fee Code	Fee (\$)		
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet.	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	420	2252	210	Extension for reply within second month	
1253	950	2253	475	Extension for reply within third month	475
1254	1,480	2254	740	Extension for reply within fourth month	
1255	2,010	2255	1,005	Extension for reply within fifth month	
1401	330	2401	165	Notice of Appeal	165
1402	330	2402	165	Filing a brief in support of an appeal	
1403	290	2403	145	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,330	2453	665	Petition to revive - unintentional	
1501	1,330	2501	665	Utility issue fee (or reissue)	
1502	480	2502	240	Design issue fee	
1503	640	2503	320	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17 (q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	2809	385	Filing a submission after final rejection (37 CFR § 1.129(a))	
1810	770	2810	385	For each additional invention to be examined (37 CFR § 1.129(b))	
1801	770	2801	385	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify)

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3)

(\$ 640)

SUBMITTED BY

Name (Print/Type)	Paul K. Legaard	Registration No. (Attorney/Agent)	38,534	Telephone	215-665-6914
Signature		Date	November 7, 2003		

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

This collection of information is required by 37 CFR 1.17 and 1.27. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1460, Alexandria, VA 22313-1460.

If you need assistance in completing this form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.

PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)		Docket Number (Optional) ISIS0057-100/ISPH-0519
In re Application of Brett P. Monia		
Application Number 09/715,983		Filed November 20, 2000
For Antisense Modulation of PI3K P85 Expression		
Art Unit 1635	Examiner Jane J. Zara	

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and appropriate non-small-entity fee are as follows (check time period desired):

- | | |
|--|-------|
| <input type="checkbox"/> One month (37 CFR 1.17(a)(1)) | \$ |
| <input type="checkbox"/> Two months (37 CFR 1.17(a)(2)) | \$ |
| <input checked="" type="checkbox"/> Three months (37 CFR 1.17(a)(3)) | \$950 |
| <input type="checkbox"/> Four months (37 CFR 1.17(a)(4)) | \$ |
| <input type="checkbox"/> Five months (37 CFR 1.17(a)(5)) | \$ |
- ☒ Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee amount shown above is reduced by one-half, and the resulting fee is: \$ 475 .
- ☐ A check in the amount of the fee is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☒ The Director has already been authorized to charge fees in this application to a Deposit Account.
- ☒ The Director is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 50-1215
- I have enclosed a duplicate copy of this sheet.

I am the ☐ applicant/inventor.

☐ assignee of record of the entire interest. See 37 CFR 3.71

Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96).

☒ attorney or agent of record. Registration Number 38,534

☐ attorney or agent under 37 CFR 1.34(a).

Registration number if acting under 37 CFR 1.34(a). _____

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

November 7, 2003

Date

(215) 665-6914

Telephone Number



Signature

Paul K. Legaard

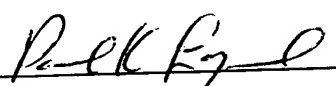
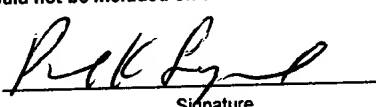
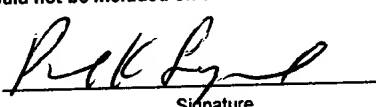
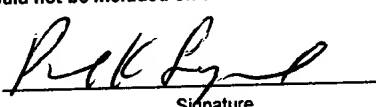
Typed or printed name

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.

☐ Total of _____ forms are submitted.

This collection of information is required by 37 CFR 1.136(a). The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 6 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

NOTICE OF APPEAL FROM THE EXAMINER TO THE BOARD OF PATENT APPEALS AND INTERFERENCES		Docket Number (Optional) ISIS0057-100/ISPH-0519								
Express Mail No.: EL 964553545 US Date of Deposit: November 7, 2003 Signature <u></u> Typed or printed name <u>Paul K. Legaard</u>	<table border="1" style="width: 100%; border-collapse: collapse;"><tr><td colspan="2" style="padding: 2px;">In re Application of Brett Monia et al.</td></tr><tr><td style="width: 50%; padding: 2px;">Application Number 09/715,983</td><td style="width: 50%; padding: 2px;">Filed November 20, 2000</td></tr><tr><td colspan="2" style="padding: 2px;">For Antisense Modulation Of PI3K P85 Expression</td></tr><tr><td style="padding: 2px;">Art Unit 1635</td><td style="padding: 2px;">Examiner Jane J. Zara</td></tr></table>		In re Application of Brett Monia et al.		Application Number 09/715,983	Filed November 20, 2000	For Antisense Modulation Of PI3K P85 Expression		Art Unit 1635	Examiner Jane J. Zara
In re Application of Brett Monia et al.										
Application Number 09/715,983	Filed November 20, 2000									
For Antisense Modulation Of PI3K P85 Expression										
Art Unit 1635	Examiner Jane J. Zara									
<p>Applicant hereby appeals to the Board of Patent Appeals and Interferences from the decision of the examiner.</p> <p>The fee for this Notice of Appeal is (37 CFR 1.17(b)) <u>\$ 330.00.</u></p> <p><input checked="" type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. Therefore, the fee shown above is reduced by half, and the resulting fee is: <u>\$ 165.00.</u></p> <p><input type="checkbox"/> A check in the amount of the fee is enclosed.</p> <p><input type="checkbox"/> Payment by credit card. Form PTO-2038 is attached.</p> <p><input checked="" type="checkbox"/> The Director has already been authorized to charge fees in this application to a Deposit Account. I have enclosed a duplicate copy of this sheet.</p> <p><input checked="" type="checkbox"/> The Director is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. <u>50-1275</u>. I have enclosed a duplicate copy of this sheet.</p> <p><input checked="" type="checkbox"/> A petition for an extension of time under 37 CFR 1.136(a) (PTO/SB/22) is enclosed.</p> <p>WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.</p> <table style="width: 100%;"><tr><td style="width: 50%; vertical-align: top; padding: 5px;"><p>I am the</p><p><input type="checkbox"/> applicant/inventor.</p><p><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)</p><p><input checked="" type="checkbox"/> attorney or agent of record. Registration number <u>38,534</u></p><p><input type="checkbox"/> attorney or agent acting under 37 CFR 1.34(a). Registration number if acting under 37 CFR 1.34(a). _____</p></td><td style="width: 50%; vertical-align: top; padding: 5px; text-align: center;"><div style="margin-bottom: 10px;"> Signature</div><div style="margin-bottom: 10px;"><u>Paul K. Legaard</u> Typed or printed name</div><div style="margin-bottom: 10px;"><u>215-665-6914</u> Telephone number</div><div><u>November 7, 2003</u> Date</div></td></tr></table> <p>NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below.</p>			<p>I am the</p> <p><input type="checkbox"/> applicant/inventor.</p> <p><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)</p> <p><input checked="" type="checkbox"/> attorney or agent of record. Registration number <u>38,534</u></p> <p><input type="checkbox"/> attorney or agent acting under 37 CFR 1.34(a). Registration number if acting under 37 CFR 1.34(a). _____</p>	<div style="margin-bottom: 10px;"> Signature</div> <div style="margin-bottom: 10px;"><u>Paul K. Legaard</u> Typed or printed name</div> <div style="margin-bottom: 10px;"><u>215-665-6914</u> Telephone number</div> <div><u>November 7, 2003</u> Date</div>						
<p>I am the</p> <p><input type="checkbox"/> applicant/inventor.</p> <p><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)</p> <p><input checked="" type="checkbox"/> attorney or agent of record. Registration number <u>38,534</u></p> <p><input type="checkbox"/> attorney or agent acting under 37 CFR 1.34(a). Registration number if acting under 37 CFR 1.34(a). _____</p>	<div style="margin-bottom: 10px;"> Signature</div> <div style="margin-bottom: 10px;"><u>Paul K. Legaard</u> Typed or printed name</div> <div style="margin-bottom: 10px;"><u>215-665-6914</u> Telephone number</div> <div><u>November 7, 2003</u> Date</div>									

☐ *Total of _____ forms are submitted.

This collection of information is required by 37 CFR 1.191. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

**RECEIVED IN THE UNITED STATES PATENT
AND TRADEMARK OFFICE**

Paper: Transmittal Form for Amendment After Final (w/Express Mail Service); Amendment After Final in response to Final Rejection dated May 7, 2003; Return Postcard all via Express Mail No. EV146 607 656US

Applicant(s): Brett P. Monia et al.

Title: ANTISENSE MODULATION OF PI3K P85 EXPRESSION

Serial No.: 09/715,983

Filed: November 20, 2000

Docket No.: ISIS0057-100 (ISPH-0519)

Date Sent: August 7, 2003

QLNguyen/Hope Graves

EV146607656US

**RECEIVED IN THE UNITED STATES PATENT
AND TRADEMARK OFFICE**

Paper: Transmittal Form for Amendment After Final (w/Express Mail Service); Amendment After Final in response to Final Rejection dated May 7, 2003; Return Postcard all via Express Mail No. EV146 607 656US

Applicant(s): Brett P. Monia et al.

Title: ANTISENSE MODULATION OF PI3K P85 EXPRESSION

Serial No.: 09/715,983

Filed: November 20, 2000

Docket No.: ISIS0057-100 (ISPH-0519)

Date Sent: August 7, 2003

QLNguyen/Hope Graves

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Delivery Date	Time	Employee Signature
Mo. Day	<input type="checkbox"/> AM <input type="checkbox"/> PM	
<input type="checkbox"/> WAIVER OF SIGNATURE (Domestic Only) Additional endorsement is void if waiver of signature is requested. If delivery employee judges that article can be left in secure address or addressee's agent (if delivery employee judges that article can be left in secure address) and I authorize that delivery employee's signature constitutes valid proof of delivery.		
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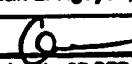
TRANSMITTAL FORM <i>(to be used for all correspondence after initial filing)</i>	Application Number	09/715,983	
	Filing Date	November 20, 2000	
	First Named Inventor	Brett P. Monia et al.	
	Art Unit	1635	
	Examiner Name	Jane J. Zara	
Total Number of Papers in This Submission	One	Attorney Docket Number	ISIS0057-100 (ISPH-0519)

ENCLOSURES (check all that apply)				
<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input checked="" type="checkbox"/> Amendment / Response <input checked="" type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/ Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Assignment Papers (for an Application) <input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s)	<input type="checkbox"/> After Allowance Communication to Group <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input type="checkbox"/> Other Enclosure(s) (please identify below):		
<table border="1" style="width: 100%;"> <tr> <td style="width: 20%;">Remarks</td> <td>Express Mail Label No. EV146 607 656US Date of Deposit: August 7, 2003</td> </tr> </table>			Remarks	Express Mail Label No. EV146 607 656US Date of Deposit: August 7, 2003
Remarks	Express Mail Label No. EV146 607 656US Date of Deposit: August 7, 2003			

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Quan Le Nguyen, Reg. No. 46,957 Cozen O'Connor, P.C.
Signature	
Date	August 7, 2003

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as Express Mail Service in an envelope addressed to: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below.			
Typed or printed name	Quan L. Nguyen, Reg. No. 46,957		
Signature		Date	August 7, 2003

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

DOCKET NO: ISIS0057-100 (ISPH-0519)

PATENT

**RESPONSE UNDER 37 CFR 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP NO. 1635**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: **Monia et al.**

Confirmation No. **6803**

Serial No.: **09/715,983**

Group Art Unit: **1635**

Filed: **November 20, 2000**

Examiner: **Zara, Jane J.**

Title: **Antisense Modulation of PI3K P85 Expression**

EXPRESS MAIL INFORMATION

**EXPRESS MAIL LABEL NO: EV 146 607 656 US
DATE OF DEPOSIT: August 7, 2003**

**MAIL STOP AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450**

Dear Sir:

AMENDMENT

In response to the Advisory Action mailed July 30, 2003, and Final Rejection mailed May 7, 2003, Applicants respectfully request that the following amendments be entered.

DOCKET NO: ISIS0057-100 (ISPH-0519)

PATENT

IN THE CLAIMS:

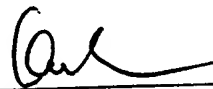
Please cancel claims 40, 42-44, 46 and 47 without prejudice.

REMARKS

Claims 24, 26-28, 30, 31, 40, 42-44, 46 and 47 are be pending. Claims 40, 42-44, 46 and 47 have been canceled. Upon entry of the amendment, claims 24, 26-28, 30 and 31 will remain pending.

In the Advisory Action mailed July 30, 2003, the Examiner indicated that claims 24, 26-28, 30 and 31 are allowable if submitted in a separate, timely filed amendment canceling non-allowable claims. Although Applicants maintain that claims 40, 42-44, 46 and 47 are also allowable, to expedite the prosecution of the application, Applicants have canceled non-allowable claims 40, 42-44, 46 and 47. Applicants respectfully request that the Examiner issue claims 24, 26-28, 30 and 31.

Respectfully submitted,



Quan L. Nguyen
Reg. No. 46,957

Dated: August 7, 2003

COZEN O'CONNOR, P.C.
1900 Market Street, 5th Floor
Philadelphia, PA 19103-3508
Telephone: (215) 665-2158
Facsimile: (215) 701-2057